Amendments to the Claims

Claims 1-53 (Cancelled)

Claim 54 (Previously Presented): A type I polyketide synthase which produces a polyketide and which comprises a loading module and a plurality of extension modules, wherein:

a) said loading module loads an optionally substituted malonyl and then effects decarboxylation of the loaded moiety to provide a corresponding optionally substituted acetyl moiety for transfer to the first of said extension modules; and

b) said loading module is of the form:

(engineered-KSq)-(AT)-(ACP), wherein:

i) ACP is an acyl carrier protein domain;

ii) AT is an acyltransferase domain which loads an optionally substituted malonyl; and

iii) engineered-KSq is a ketosynthase (KS) domain which effects decarboxylation of a loaded optionally substituted malonyl, wherein said engineered-KSq domain is obtained by replacing the active site cysteine of a KS domain of an extension module with a glutamine;

wherein the polyketide produced by the polyketide synthase is other than a 14-membered macrolide having a 13-methyl group due to incorporation of an unsubstituted acetate starter.

Claim 55 (Previously Presented): A type I polyketide synthase according to claim 54, wherein said acyltransferase domain has an arginine residue in the active site.

Claim 56 (Currently Amended): A type I polyketide synthase according to claim 55, wherein said acyltransferase domain is an ~~natural~~ extension module acyltransferase domain.

Claim 57 (Currently Amended): A type I polyketide synthase according to claim 54, wherein said ketosynthase domain which

is the source of said ~~the~~ engineered-KSq and said acyltransferase domain ~~pair produced by mutation~~ occur together in an extension module ~~in their unaltered state~~.

Claim 58 (Previously Presented): A type I polyketide synthase according to claim 55, wherein said acyltransferase domain is specific for loading with malonyl.

Claim 59 (Previously Presented): A type I polyketide synthase according to claim 55, wherein said acyltransferase domain is specific for loading with methylmalonyl.

Claim 60 (Previously Presented): A type I polyketide synthase according to claim 55, wherein said acyltransferase domain is the acyltransferase domain of extension module 5 of the spiramycin polyketide synthase.

Claim 61 (Previously Presented): A type I polyketide synthase according to claim 56, wherein said acyltransferase domain is the acyltransferase of module 6 of the niddamycin polyketide synthase.

Claim 62 (Previously Presented): A type I polyketide synthase according to claim 56, wherein said acyltransferase domain is the acyltransferase of module 4 of the FK506 polyketide synthase.

Claim 63 (Previously Presented): A type I polyketide synthase according to claim 54, wherein said polyketide synthase is effective to synthesize a polyketide selected from

(a) 12- and 16-membered macrolides with acetate starter units;

(b) 12, 14, and 16-membered macrolides with propionate starter units;

(c) variants of rifamycin, avermectin, rapamycin,

immunomycin and FK506 which differ from the natural compound in the incorporation of acetate starter units or propionate starter units;

(d) a polyketide wherein the starter unit is derived by the action of said engineered-KSq domain on the enzyme-bound product of said AT domain, wherein said AT domain is from extension module 4 of the FK506 polyketide synthase; or

(e) a polyketide wherein the starter unit is derived by the action of said engineered-KSq domain on the enzyme-bound product of said AT domain, wherein said AT domain is from ~~of~~ extension module 6 of the niddamycin polyketide synthase.

Claim 64 (Previously Presented): A type I polyketide synthase which produces a polyketide and which comprises a loading module and a plurality of extension modules, wherein:

a) said loading module loads an optionally substituted malonyl and then effects decarboxylation of the loaded moiety to provide a corresponding optionally substituted acetyl moiety for transfer to the first of said extension modules; and

b) said loading module is of the form:

(KSq)-(AT)-(ACP), wherein:

i) ACP is an acyl carrier protein domain;

ii) AT is an acyltransferase domain which loads an optionally substituted malonyl and is selected from the group consisting of the acyltransferase domain of module 6 of the niddamycin polyketide synthase, the acyltransferase domain of module 4 of the FK506 polyketide synthase, and the acyltransferase domain of module 5 of the spiramycin polyketide synthase; and

iii) KSq is a domain which effects decarboxylation of a loaded optionally substituted malonyl and which differs from a ketosynthase domain of an extension module by having a glutamine residue in place of the cysteine residue in the active site;

wherein the polyketide produced by the polyketide synthase is other than a 14-membered macrolide having a 13-methyl group due to incorporation of an unsubstituted acetate starter.

Claim 65 (Currently Amended): The type I polyketide synthase according to claim 64, wherein ~~(AT)~~ said AT is the acyltransferase domain of module 6 of the niddamycin polyketide synthase,

Claim 66 (Currently Amended): The type I polyketide synthase according to claim 64, wherein ~~(AT)~~ said AT is the acyltransferase domain of module 4 of the FK506 polyketide synthase.

Claim 67 (Cancelled)

Claim 68 (Currently Amended): The type I polyketide synthase according to claim 64, wherein ~~(AT)~~ said AT is the acyltransferase domain of module 5 of the spiramycin polyketide synthase.

Claims 69-74 (Cancelled)

Claim 75 (Previously Presented): A type I polyketide synthase which produces a 12- or 14- membered macrolide and which comprises a loading module and a plurality of extension modules, wherein:

a) said loading module is the loading module of the tylosin polyketide synthase; and

b) at least the first of said extension modules is not naturally associated with said loading module;

wherein the polyketide produced by the polyketide synthase is other than a 14-membered macrolide having a 13-methyl group due to incorporation of an unsubstituted acetate starter.

Claim 76 (Cancelled)

Claim 77 (New): A type I polyketide synthase according to claim 54, wherein said ketosynthase domain which is the source of said ~~the~~ engineered-KSq and said acyltransferase domain are from different polyketide synthases.